Section: Critical Care Medicine

Original Research Article

# ANALYSIS OF EFFECT OF DEXMEDETOMIDINE ON VENTILATOR FREE DAYS AND MORTALITY IN SEPSIS PATIENTS RECEIVING MECHANICAL VENTILATION

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ABSTRACT

**Background:** Sepsis accounts for nearly 70% of all instances of acute respiratory distress syndrome (ARDS). Dexmedetomidine, a highly selective α2-adrenergic agonist, stands out as a distinctive sedative compared to γ-aminobutyric acid receptor agonists. Hence; the present study was conducted to analyze the effect of dexmedetomidine on ventilator free days and mortality in sepsis patients receiving mechanical ventilation.

**Materials and Methods:** A total of 100 patients who were aged 20 years or older, had sepsis, and needed mechanical ventilation for at least 24 hours were included in the present study. Mechanical ventilation encompassed both invasive and noninvasive methods. Sepsis was characterized as a systemic inflammatory response syndrome resulting from an infection. All participants were randomly assigned to receive either a sedation protocol incorporating dexmedetomidine or one that excluded it. Sedation was sustained throughout the mechanical ventilation period or as required. The co-primary outcomes assessed were 28-day mortality and the number of ventilator-free days. All data were systematically recorded in a Microsoft Excel spreadsheet and subsequently analyzed using SPSS software.

**Results:** Overall, 28-day mortality was seen in 14 percent and 22 percent of the patients of Dexmedetomidine Group and Non-Dexmedetomidine Group respectively. Median ventilator free days among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 21 days and 19 days respectively. Median ICU stay among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 8 days and 9 days respectively. Non-significant results were obtained while comparing the outcome among the two study groups.

**Conclusion:** In patients who necessitate mechanical ventilation, the administration of dexmedetomidine, in contrast to its absence, did not yield a statistically significant enhancement in either mortality rates or the number of days free from ventilation.

**Keywords:** Dexmedetomidine, Ventilator, Sepsis.

## INTRODUCTION

Sepsis accounts for nearly 70% of all instances of acute respiratory distress syndrome (ARDS). Furthermore, it heightens the risk of ventilator-induced lung injury. As a result, there is a pressing need for the formulation of a ventilatory strategy that ensures sufficient oxygenation while minimizing lung damage in patients suffering from acute infections. This represents a crucial therapeutic opportunity to enhance patient outcomes. Inadequate ventilatory settings not only pose a risk to lung health but may also exacerbate the progression of organ failure in sepsis through inter-organ communication.[1,2] Despite the significant association between sepsis and lung

injury, the majority of research focusing on mechanical ventilation strategies in ARDS has not specifically targeted patients with sepsis-related ARDS. As a consequence, most guidelines for mechanical ventilation in sepsis patients are extrapolated from ARDS studies that encompassed a variety of clinical conditions. Although there have been notable advancements in general ventilatory management applicable to all critically ill individuals, the unique aspects of sepsis-related lung injury may necessitate tailored approaches in clinical practice.[3-5]

Dexmedetomidine, a highly selective α2-adrenergic agonist, stands out as a distinctive sedative compared to γ-aminobutyric acid receptor agonists. This agent enhances patients' capacity to articulate their pain levels more effectively than midazolam and propofol. Consequently, dexmedetomidine appears to be advantageous for achieving light sedation. Its analgesic properties, along with the potential to mitigate the effects of other sedatives that may induce delirium, could contribute to a reduction in both agitation and delirium.[6-8] Hence; the present study was conducted to analyze the effect of dexmedetomidine on ventilator free days and mortality in sepsis patients receiving mechanical ventilation.

## MATERIALS AND METHODS

The present study was conducted to analyze the effect of dexmedetomidine on ventilator free days and mortality in sepsis patients receiving mechanical ventilation. A total of 100 patients who were aged 20 years or older, had sepsis, and needed mechanical ventilation for at least 24 hours were included in the present study. Mechanical ventilation encompassed both invasive and noninvasive methods. Sepsis was characterized as a systemic inflammatory response syndrome resulting from an infection. All participants were randomly assigned to receive either a sedation protocol incorporating dexmedetomidine or one that excluded it. Comprehensive demographic and clinical information for all patients was collected. The control group was administered sedative agents such as propofol and midazolam, along with analgesics, without the inclusion of dexmedetomidine. The sedation depth aimed for a Richmond Agitation-Sedation Scale (RASS) score of 0 (indicating calmness) during daytime and a RASS score of −2 (indicating light sedation) at night for both groups. Sedation was sustained throughout the mechanical ventilation period or as required. The co-primary outcomes assessed were 28-day mortality and the number of ventilator-free days. All data were systematically recorded in a Microsoft Excel spreadsheet and subsequently analyzed using SPSS software.

## RESULTS

The mean age of the patients of the Dexmedetomidine Group and Non-Dexmedetomidine Group was 61.3 years and 63.7 years respectively. Majority proportion of patients of both the study groups were males. Mean CRP levels among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 14.3 mg/dL and 17.1 mg/dL respectively. Overall, 28-day mortality was seen in 14 percent and 22 percent of the patients of Dexmedetomidine Group and Non-Dexmedetomidine Group respectively. Median ventilator free days among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 21 days and 19 days respectively. Median ICU stay among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 8 days and 9 days respectively. Non-significant results were obtained while comparing the outcome among the two study groups.

**Table 1: Patient's details**

| Variable | Dexmedetomidine Group (n=50) | Non-Dexmedetomidine Group (n=50) |
|---|---|---|
| **Mean age (years)** | 61.3 | 63.7 |
| **Males (n)** | 29 | 31 |
| **Females (n)** | 21 | 19 |
| **Mean Body weight (Kg)** | 53.3 | 55.7 |
| **Mean CRP (mg/dL)** | 14.3 | 17.1 |
| **Mean procalcitonin (ng/mL)** | 15.9 | 14.7 |
| **Overall median SOFA Score** | 9 | 9 |

**Table 2: Outcome measurements and adverse events**

| Outcome | Dexmedetomidine Group (n=50) | Non-Dexmedetomidine Group (n=50) | p-value |
|---|---|---|---|
| **28- day mortality** | 7 (14 %) | 11 (22 %) | 0.12 |
| **Ventilator free days (Median)** | 21 | 19 | 0.28 |
| **ICU stay (Median)** | 8 | 9 | 0.37 |

## DISCUSSION

Mechanical ventilation is one of the cornerstones of critical care and one of the most frequent life support measures used in severely ill patients. The history of intensive care units is deeply linked to the development of mechanical ventilation support. Providing adequate respiratory support through mechanical ventilation has evolved from an

understanding of normal respiratory physiology and gas exchange, histological and biomolecular evaluation of lung tissue, and the development of reliable and user-friendly mechanical ventilators. Maximum benefit requires well-defined mechanical ventilator support strategies. While developing such strategies is surely a challenge, important observational studies and randomized controlled trials have provided the results on which these strategies could be based. Sepsis also presents a formidable clinical challenge. Sepsis is a major syndromic cause for intensive care unit admission, and sepsis is associated with high morbidity and mortality.[9,10] Dexmedetomidine received approval from the Food and Drug Administration in late 1999 for human use as a short-term agent (less than 24 hours) for analgesia and sedation within the intensive care unit (ICU). Its distinctive characteristics make it particularly effective for sedation and analgesia throughout the entire perioperative period. While its roles as a premedication, an adjunct to general and regional anesthesia, and a postoperative sedative and analgesic are comparable to those of benzodiazepines, a more detailed examination indicates that this α2-adrenoceptor agonist offers more advantageous side effects.[11] Hence; the present study was conducted to analyze the effect of dexmedetomidine on ventilator free days and mortality in sepsis patients receiving mechanical ventilation.

The mean age of the patients of the Dexmedetomidine Group and Non-Dexmedetomidine Group was 61.3 years and 63.7 years respectively. Majority proportion of patients of both the study groups were males. Mean CRP levels among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 14.3 mg/dL and 17.1 mg/dL respectively. Overall, 28-day mortality was seen in 14 percent and 22 percent of the patients of Dexmedetomidine Group and Non-Dexmedetomidine Group respectively. Kawazoe Y et al examined whether a sedation strategy with dexmedetomidine can improve clinical outcomes in patients with sepsis undergoing ventilation. Patients were randomly assigned to receive sedation with dexmedetomidine (n = 100) or to a control group receiving sedation without dexmedetomidine (n = 101). Both groups were administered additional agents, including fentanyl, propofol, and midazolam. The primary outcomes of interest were mortality and the number of ventilator-free days within a 28-day period. Secondary outcomes included the Sequential Organ Failure Assessment score measured on days 1, 2, 4, 6, and 8, sedation management, incidence of delirium and coma, length of stay in the intensive care unit, renal function, inflammatory markers, and nutritional status. Out of 203 patients screened, 201 were successfully randomized. The average age of participants was 69 years (SD, 14 years), with 63% being male. There was no significant difference in 28-day mortality rates between the dexmedetomidine and control groups. Similarly, the number of ventilator-free days did not differ significantly between the two groups. However, the dexmedetomidine group exhibited a significantly higher rate of well-controlled sedation during mechanical ventilation, while other outcomes showed no significant differences. Adverse events were reported in 8 (8%) patients in the dexmedetomidine group and 3 (3%) patients in the control group.[12]

Median ventilator free days among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 21 days and 19 days respectively. Median ICU stay among patients of Dexmedetomidine Group and Non-Dexmedetomidine Group was 8 days and 9 days respectively. Non-significant results were obtained while comparing the outcome among the two study groups. Chen P et al reviewed the extant literature in DEX and determine its influence on ventilation time in adult septic patients. Databases of PubMed, Cochrane, and EMBASE were applied till 20th January 2019 without language restriction. The searching strategy as following: sepsis OR septic AND mechanical ventilation AND dexmedetomidine. Four studies with a total of 349 patients were included. Three trials with 267 patients revealed the effect of DEX on duration of mechanical ventilation, two trials with 264 patients on ventilator-free days and four trials with 334 patients on 28-day mortality. The analyzed results indicated that DEX was not associated with significantly different durations of mechanical ventilation. However, there were significant differences in ventilator-free days and 28-day mortality in the septic patients. Administration of DEX for sedation in septic patients was not associated with the duration of mechanical ventilation, but it increased the ventilator-free days and reduced 28-day mortality.[13]

## CONCLUSION

In patients who necessitate mechanical ventilation, the administration of dexmedetomidine, in contrast to its absence, did not yield a statistically significant enhancement in either mortality rates or the number of days free from ventilation.

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